

PRENATAL PROBIOTIC FORMULATIONS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application No. 62/714,589, filed Aug. 3, 2018, the content of which is hereby incorporated by reference in its entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Aug. 1, 2019, is named 106887-7560_SL.txt and is 10,964 bytes in size.

TECHNICAL FIELD

[0003] This disclosure relates to novel probiotic formulations and methods for using same for treating or preventing prenatal illness.

BACKGROUND

[0004] Necrotizing enterocolitis (NEC) is a highly fatal disease that typically occurs in premature babies. Treatments are limited, and symptoms can progress rapidly, thus making prevention ideal. This disclosure provides such treatments.

SUMMARY

[0005] Provided herein is a novel probiotic delivery system in which *Lactobacillus reuteri* (Lr) is delivered in a biofilm state, that protects the intestines from NEC.

[0006] In one aspect, provided herein is a prenatal method for one or more of: promoting health, maintaining gut homeostasis, treating disease, or preventing a disease, conferring prenatal immunity, each suitably treated or conferred by the formation or enhancement of a biofilm in a fetus, the method comprising, or alternatively consisting essentially of, or yet further consisting of, prenatal administration to a pregnant female carrying the fetus an effective amount of a microsphere comprising a biofilm-generating probiotic bacterium and a prebiotic, wherein the prebiotic comprises a nutritional supplementation for the probiotic bacterium.

[0007] Also provided herein is a prenatal method of administering a probiotic to a fetus comprising, or consisting essentially of, or consisting of, administering to a pregnant female carrying the fetus an effective amount of a microsphere comprising or alternatively consisting essentially of, or yet further consisting of a biofilm-generating probiotic bacterium and a prebiotic, wherein the prebiotic comprises a nutritional supplementation for the probiotic bacterium.

[0008] Yet further provided is a prenatal method of conferring NEC resistance or immunity to a fetus, the method comprising, or alternatively consisting essentially of, or consisting of, administering to a pregnant female carrying the fetus an effective amount of a microsphere comprising a biofilm-generating probiotic bacterium and a prebiotic, wherein the prebiotic comprises a nutritional supplementation for the probiotic bacterium.

[0009] In the above methods, the microsphere further comprises, or alternatively consists essentially of, or yet further consists of, a partial or complete biofilm coating on the external surface of the microsphere. In another aspect,

the microsphere comprises, or alternatively consists essentially of, or yet further consists of a material selected from the group of: a biodegradable polymer, a non-degradable polymer, a metal, and wherein the diameter of the microsphere is from about 0.5 microns to about 1,000 microns. In a further aspect, the composition further comprises, or alternatively consists essentially of, or yet further consists of one or more of: a prebiofilmic, a therapeutic drug or agent, a chemical reductant, a molecule that promotes adsorption, a molecule that supports absorption. In a yet further aspect, the prebiofilmic comprises, or alternatively consists essentially of, or yet further consists of an agent that supports biofilm formation and durability.

[0010] In a further aspect, the prebiofilmic is a DNA binding polypeptide or protein and/or a DNABII polypeptide or protein or an equivalent of each thereof.

[0011] In a yet further aspect, the prebiotic comprises, or alternatively consists essentially of, or yet further consists of a water-soluble carbohydrate, inulin, oligosaccharides, oligofructose, fructo-oligosaccharide, galacto-oligosaccharide, glucose, starch, maltose, maltodextrins, polydextrose, amylose, sucrose, fructose, lactose, isomaltulose, polyols, glycerol, carbonate, thiamine, choline, histidine, trehalos, nitrogen, sodium nitrate, ammonium nitrate, phosphorus, phosphate salts, hydroxyapatite, potassium, potash, sulfur, homopolysaccharide, heteropolysaccharide, cellulose, chitin, vitamins, and combination thereof.

[0012] In a further aspect, the microsphere is administered in a pharmaceutically acceptable carrier or a biocompatible scaffold.

[0013] Non-limiting examples of the probiotic bacterium include one or more of *L. acidophilus*, *L. crispatus*, *L. gasseri*, group *L. delbrueckii*, *L. salivarius*, *L. casei*, *L. paracasei*, *L. plantarum*, *L. rhamnosus*, *L. reuteri*, *L. brevis*, *L. buchneri*, *L. fermentum*, *L. rhamnosus*, *B. adolescentis*, *B. angulation*, *B. bifidum*, *B. breve*, *B. catenulatum*, *B. infantis*, *B. lactis*, *B. longum*, *B. pseudocatenulatum*, *S. thermophiles*, *Pseudomonas fluorescens*, *P. protegens*, *P. brassicacearum*, *P. aeruginosa*, *Azospirillum. brasiliense*, *A. lipferum*, *A. halopraeferens*, *A. irakense*, *Acetobacter diazotrophicus*, *Herbaspirillum seropedicae*, *Bacillus subtilis*, *Pseudomonas stutzeri*, *fluorescens*, *P. putida*, *P. cepacian*, *P. vesicularis*, *P. paucimobilis*, *Bacillus cereus*, *B. thuringiensis*, *B. sphaericus*, *Shewanella oneidensis*, *Geobacter bemidjensis*, *G. metallireducens*, *G. sulfurreducens*, *G. uraniireducens*, *G. lovleyi*, *Serratia marcescens*, *Desulfovibrio vulgaris*, *D. desulfuricans*, *Dechloromonas aromatic*, *Deinococcus radiodurans*, *Methylibium petroleiphilum*, *Alcanivorax borkumensis*, *Archaeglobus fulgidus*, *Haloflexax* sp., *Halobacterium* sp., and combinations thereof.

[0014] In a further aspect, the probiotic bacterium provides one or more of supporting anti-bacterial immunity, correcting dysbiosis, enhancing or supporting the gastrointestinal barrier, supporting or enhancing gastrointestinal motility, localized release of antibiotic compositions, or antagonizing disease-related bacterial infections.

[0015] In another aspect, the probiotic bacterium prevents pathogen colonization and/or limits excessive inflammatory responses by down-regulating cytokine and chemokine production.

[0016] In another aspect, the microsphere comprises a solid core or a hollow core. In a particular aspect, the prebiotic is encapsulated within the hollow core.